

Appl. No. : known
Filed : July 2, 1998

domain comprising an amino acid sequence [substantially] as set out as residues 99 to 106 of SEQ ID NO: 2.

2. An [isolated] antibody comprising a specific binding member according to claim 1, which further comprises the polypeptide domains [substantially] as set out as residues 31-36 and 51-66 of SEQ ID NO: 2.

3. An [isolated] antibody comprising a specific binding member according to claim 2, wherein said binding domains are carried by a human antibody framework.

4. An [isolated] antibody comprising a specific binding member according to claim 3, which comprises [substantially] the polypeptide sequence of SEQ ID NO: 2.

5. An [isolated] antibody comprising a specific binding member [capable of binding an intracellular antigen, wherein said] which comprises a first specific binding member [comprises a polypeptide binding domain] comprising an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 2 in association with a second specific binding member comprising an amino acid sequence [substantially] as set out as residues 88 to 98 of SEQ ID NO: 4.

6. An [isolated] antibody comprising a specific binding member [according to claim 5 which further comprises] which comprises a first specific binding member comprising an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 2 in association with a second specific binding member comprising the polypeptide binding domains [substantially] as set out as residues 23-33 and 49-55 of SEQ ID NO: 4.

7. An [isolated] antibody comprising a specific binding member [according to claim 6 wherein said binding domains are carried by a human antibody framework] which comprises a first specific binding member comprising an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 2 in association with a second specific binding member comprising the polypeptide sequence of SEQ ID NO: 4.

Appl. No. : known
Filed : July 2, 1998

8. An [isolated] antibody comprising a specific binding member [according to claim 7] which comprises [substantially] a first specific binding member comprising an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 2 in association with a second specific binding member comprising the polypeptide [sequence] binding domains as set out as residues 23-33 and 49-55 of SEQ ID NO: 4, wherein said binding domains are carried by a human antibody framework.

9. An antibody comprising a specific binding member according to Claim 8 in the form of an antibody F(ab')₂ or scFv fragment [which comprises a first specific binding member as defined in any one of claims 1 to 4 in association with a second specific binding member as defined in any one of claims 5 to 8].

10. An antibody comprising a specific binding member according to Claim [9] 1, [in the form of an antibody F(ab')₂ or scFv fragment] wherein said antibody carries a label selected from the group consisting of a detectable label and a functional label.

11. An isolated nucleic acid which comprises a sequence encoding a specific binding member [according to any one of claims 1 to 10 which carries a detectable or functional label] as defined in Claim 1.

12. A method of preparing an antibody comprising [An isolated nucleic acid which comprises a sequence encoding] a specific binding member [as defined in any one of claims 1 to 11] that comprises a polypeptide binding domain comprising an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 2, said method comprising the steps of

expressing a nucleic acid which comprises a sequence encoding a specific binding member as defined in Claim 1 under conditions to bring about expression of said binding member, and

recovering the binding member.

13. [A method of preparing] An antibody comprising a specific binding member [as defined in any one of claims 1 to 11 which comprises expressing the nucleic acid of claim 12 under

Appl. No. : known
Filed : July 2, 1998

conditions to bring about expression of said binding member, and recovering the binding member] according to Claim 1 for use in a method of treatment or diagnosis of the human or animal body.

14. A method of preparing an antibody comprising a specific binding member [according to any one of claims 1 to 11 for use in a method of treatment or diagnosis of the human or animal body] capable of binding an intracellular antigen, which method comprises:

- a) providing a starting repertoire of nucleic acids encoding a VH domain which lacks a CDR3 encoding region;
- b) combining said repertoire with a donor nucleic acid encoding an amino acid sequence as set out as residues 99 to 106 of SEQ ID NO: 1 such that said donor nucleic acid is inserted into the missing CDR3 region, so as to provide a product repertoire of nucleic acids encoding a VH domain;
- c) expressing the nucleic acids of said product repertoire;
- d) selecting a specific binding member which has a maximum tumour:blood localization ratio in a test animal of greater than 3:1; and
- e) recovering said binding member or the nucleic acid encoding said binding member.

15. A method of preparing an antibody comprising a specific binding member capable of binding an intracellular antigen, which method comprises:

- a) providing a starting repertoire of nucleic acids encoding a VH domain which lacks a CDR3 encoding region;
- b) combining said repertoire with a donor nucleic acid encoding an amino acid sequence [substantially] as set out as residues 99 to 106 of SEQ ID NO: 1 such that said donor nucleic acid is inserted into the missing CDR3 region, so as to provide a product repertoire of nucleic acids encoding a VH domain;
- c) expressing the nucleic acids of said product repertoire; [and]
- d) selecting a specific binding member which has a maximum tumour:blood [localisation] localization ratio in a test animal of [$>$] greater than 3:1, and [optionally] at said ratio, [an] has a minimum organ to blood ratio of [$<$] less than 1:1; and

Appl. No. : known
Filed : July 2, 1998

e) recovering said binding member or the nucleic acid encoding [it] said binding member.

16. A method of treatment of a tumour in a human patient which comprises administering to said patient an effective amount of an antibody comprising a specific binding member as defined in [any one of claims] Claim 1 [to 11].

PLEASE ADD new Claim 17, as follows:

17. An antibody comprising a specific binding member which comprises a first specific binding member comprising an amino acid sequence as set out as residues 31-36, 51-66 and 99 to 106 of SEQ ID NO: 2 in association with a second specific binding member comprising an amino acid sequence as set out as residues 88 to 98 of SEQ ID NO: 4.

Please charge any additional fees or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 21, 2000

By: Joseph M. Reisman

Joseph M. Reisman
Registration No. 43,878
Attorney of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(619) 235-8550

AMEND
S:\DOCS\JLD\JLD-1110.DOC
122000